



NTP
National Toxicology Program

NTP Board of Scientific Counselors Technical Reports Review Subcommittee

Report from the September 27-28, 2005 Meeting





Dibromoacetic acid

Water disinfection by-product

Sex/Species	Evidence	Neoplastic lesions
MR	SE	Malignant mesothelioma
FR	SE	Mononuclear cell leukemia
MM	CE	Hepatocellular neoplasms, hepatoblastoma (Lung neoplasms)
FM	CE	Hepatocellular neoplasms, (Lung neoplasms)



Divinylbenzene

Used in adhesives, plastics, coatings as copolymer and cross linking agent

Sex/Species	Evidence	Neoplastic lesions
MR	EE	Renal carcinoma, Brain tumors (glial)
FR	NE	-
MM	NE	-
FM	EE	Alveolar / bronchiolar adenoma or carcinoma



Methyl isobutyl ketone

Denaturant in alcohol, solvent in industrial extractions and synthetic reactions

Sex/Species	Evidence	Neoplastic lesions
MR	SE	Renal tubular neoplasms; (Mononuclear cell leukemia)
FR	EE	Renal mesenchymal neoplasms
MM	SE	Hepatocellular neoplasms
FM	SE	Hepatocellular neoplasms



Diisopropyldicarbodiimide

Coupling and condensing agent used in the synthesis of polypeptides

Sex/Species	Evidence	Neoplastic lesions
MR	NE	-
FR	NE	-
MM	NE	-
FM	NE	-



Methylimidazole

Manufacture of pharmaceuticals, agricultural chemicals and dyes; found in foods and tobacco smoke

Sex/Species	Evidence	Neoplastic lesions
MR	NE	-
FR	EE	Mononuclear cell leukemia
MM	CE	Alveolar/bronchiolar neoplasms
FM	CE	Alveolar/bronchiolar neoplasms



Photocarcinogenicity study of glycolic or salicylic acid in SKH-1 mice exposed to simulated solar light (SSL)

Exposure	Outcome	Effect
SSL	Skin neoplasms	Positive control
SSL + cream	Skin neoplasms	Decreased latency
SSL + glycolic acid	Skin neoplasms	No effect*
SSL + salicylic acid	Skin neoplasms	Photoprotective*

* Compared to the SSL + cream



Genetically Modified Models - p53^{+/-} mice

Substance	Exposure route	Sex	Evidence	Lesions
Dichloroacetic acid	Drinking Water	M and F	NE	No lesions
Bromodichloromethane	Drinking Water	M	NE	Renal tubule degeneration
	Drinking Water	F	NE	Fatty changes in hepatocytes
	Gavage	M	NE	Renal tubule degeneration
	Gavage	F	NE	Fatty changes in hepatocytes
Sodium bromate	Drinking Water	M and F	NE	No lesions
Diisopropylcarbodiimide	Dermal	F	NE	No lesions



Genetically Modified Models - Tg.AC mice

Substance	Exposure route	Sex	Lesions
Dichloroacetic acid	Dermal	M and F	Squamous cell papilloma
	Drinking Water	M and F	Alveolar/bronchial adenoma
Bromodichloro-methane	Dermal	M and F	No lesions
	Gavage	M	Nephropathy
	Gavage	F	Forestomach papillomas
	Drinking Water	M	Nephropathy
	Drinking Water	F	Cytoplasmic vacuolization of hepatocytes



Genetically Modified Models - Tg.AC mice

Substance	Exposure route	Sex	Lesions
Sodium bromate	Dermal	M and F	Non-neoplastic lesions in thyroid gland and kidney
	Drinking Water	M and F	Non-neoplastic lesions in thyroid gland and kidney
Diisopropyl-carbodiimide	Dermal	F	No lesions



Outcome from Genetically Modified Models vs. Bioassay

	Tg.AC	p53	Bioassay
Dichloroacetic acid			
Drinking water	+	-	+
Dermal	+	ND	ND
Bromodichromethane			
Drinking water	-	-	-
Dermal	-	ND	ND
Gavage	+	-	+
Sodium Bromate			
Drinking water	-	-	+ *
Dermal	-	ND	ND
Diisopropylcarbodiimide			
Dermal	- **	- **	-

* KBr

** 5 months exposure; rest are 6 and/or 9 month exposure



Future Reviews of Technical Reports

Reviewed June 12, 2006

- **Genistein - Multigenerational Study**
- **Genistein - Bioassay**
- **α -Methylstyrene**
- **Methylene Blue Trihydrate**

For Review August 28, 2006- Genetically Modified Models

- **Allyl Bromide**
- **Benzene**
- **Dicyclohexylcarbodiimide**
- **Glycidol**
- **Phenolphthalein**